Nutrition in Clinical Practice
Volume 35 Number 4
August 2020 697–702
© 2019 The Authors. *Nutrition in Clinical Practice* published by Wiley Periodicals, Inc. on behalf of American Society for Parenteral and Enteral Nutrition
DOI: 10.1002/ncp.10436
wileyonlinelibrary.com

Optimizing Delivery of Breast Milk for Premature Infants: Comparison of Current Enteral Feeding Systems

Khaled Abdelrahman, BS[1]; Jane Jarjour, MD[2]; Joseph Hagan, ScD[3]; Heeju Yang, BS[3]; Danielle Sutton, MPH[3]; and Amy Hair, MD[3]

Abstract

Background: Incomplete delivery of fat from expressed breast milk (EBM) during enteral feeding to premature neonates remains a significant problem. Feeding system manufacturers have introduced changes to the enteral syringe design to improve fat delivery that have not yet been evaluated in the literature. *Methods:* This study compares percentage delivery of fat from EBM using 2 major enteral feeding systems in various configurations with silicone and polyurethane tubing material and ENFit and Legacy connection systems at 3 clinically relevant infusion rates. *Results:* The percent of fat delivery from EBM was significantly higher for the eccentric syringe system than the concentric system ($P = 0.036$) but did not vary significantly across infusion rates ($P = 0.081$). Silicone tubing had a significantly higher percent of fat delivery than polyurethane tubing within the eccentric syringe system ($P = 0.039$) but did not vary significantly across infusion rates ($P = 0.105$). There was no significant difference between ENFit and Legacy connectors using eccentric syringes with silicone tubing ($P = 0.360$). *Conclusion:* We demonstrate that changes to syringe design and tubing material are effective and improve fat delivery from EBM, which may result in improved growth and outcomes in premature infants. The eccentric syringe marginally improves fat delivery in comparison with the concentric syringe, and silicone tubing significantly improves fat delivery compared with polyurethane tubing. (*Nutr Clin Pract.* 2020;35:697–702)

Keywords

dietary fats; ENFit; enteral nutrition; human milk; neonate; premature infant; syringes

Introduction

Approximately half of the caloric content of expressed breast milk (EBM) comes from fat, and thus adequate fat intake is critical to ensuring appropriate energy provision to the neonates.[1,2] Because of its high energy density compared with other macronutrients such as proteins and carbohydrates, fat from EBM is an effective energy source even over the relatively small volume of enteral feeds provided to premature infants in the neonatal intensive care unit (NICU).[3,4] Additionally, because premature infants have particularly low energy reserves because of shortened gestation and limited body fat and liver glycogen storage, the fat content of EBM ensures maintenance of the infant's existing energy supplies and prevents postnatal deficits in essential macronutrients.[5-7] Infants who receive enteral feeds also depend on the fat content of EBM for the role fat plays in basic physiologic functions such as organogenesis and development, cellular communication and metabolism, and immune function.[6,7,10] Furthermore, fat from EBM in enteral feeds is crucial to premature infants in the NICU, as appropriate weight gain velocity, which depends on nutrition support, has been linked to long-term outcomes such as neurodevelopment.[7-9] The risk of abnormal cognitive and neurodevelopmental outcomes associated with caloric deficits for premature infants is additionally highlighted by nutrition recommendations for aggressive early nutrition by the American Academy of Pediatrics Committee on Nutrition.[11]

Despite the importance of fat in EBM for premature infants in the NICU, significant losses of EBM fat concentration during enteral feeding has been described dating back to the 1980s, with recent studies showing that

---

From the [1]Dell Medical School, University of Texas at Austin, Austin, Texas, USA; [2]Department of Pediatrics, University of Colorado School of Medicine, Denver, Colorado, USA; and the [3]Department of Pediatrics, Section of Neonatology, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA.

Financial disclosure: None declared.

Conflicts of interest: None declared.

This article originally appeared online on November 11, 2019.

Corresponding Author:
Amy Hair, MD, Department of Pediatrics, Section of Neonatology, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA.
Email: abhair@bcm.edu

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

this still remains a major impediment in NICU enteral feeding.[15,16] The incomplete delivery of fat from EBM has been attributed to separation of fat and other nutrients from aqueous milk components and subsequent adherence to the feeding syringe and tubing over the course of infusion.[12] Recent studies looking at nutrient loss in enteral tube feeding have found that different feeding methods (bolus over continuous) and fortification of feeds (human milk–based fortifier with cream over bovine milk–based fortifier) all affect nutrient delivery, demonstrating that there are many factors that affect optimal delivery of nutrients in enteral feeding.[14-17]

The persistence of these fat losses from EBM may also be related to limited design changes in enteral feeding systems and the variable clinical practices between institutions. Although numerous interventions have been shown to decrease fat losses from EBM during enteral feeds, including tilting the syringe nozzle, using shorter feeds and shorter connecting tubes, and supplementing EBM with fortifier and cream, few of these changes have been applied consistently in the clinical setting.[14-18] Most NICUs feed EBM through a concentric syringe on a horizontally oriented pump with polyurethane enteral tubing, but practices still vary from site to site with individual hospital milk banks and NICUs following unique protocols for preparation and administration of feeds.

With advancements in materials science and analytical methods for assessing total milk fat content, feeding system manufacturers have recently begun to introduce changes to their feeding systems with the goal of eliminating fat losses in the delivery of EBM in enteral feeds through mechanical syringe pump feeding systems. For example, 1 new feeding system utilizes an enteral syringe with an off-center or "eccentric" tip, in contrast to the concentric syringe, which is currently most widely utilized.[19] Examples of these syringe types are depicted in Figure 1. This eccentric syringe also has a polypropylene plunger head that is flatter than previous syringes with an O-ring style gasket, which is designed to reduce fat adherence to the plunger head.[19] Fat delivery using the eccentric syringe nozzle has been compared with the concentric syringe nozzle as early as 1984, when Narayanan et al demonstrated that a version of the eccentric syringe nozzle decreased fat losses in delivery of EBM as compared with the concentric syringe.[14] One theory behind improved fat delivery from EBM using an eccentric syringe nozzle is that the eccentric nozzle directs the flow of milk "upwards," corresponding with the flow of the fat that has separated from the rest of the milk contents.[14] However, these changes were not adopted by major enteral feeding system manufacturers prior to the current eccentric syringe system, the efficacy of which has not been investigated in the literature prior to this study.

Figure 1. Depiction of concentric (left) and eccentric (right) syringes.

Another design modification introduced into the enteral feeding market by manufacturers is the use of silicone tubing instead of the traditional polyurethane enteral tubing, which is most commonly used. This change aims to minimize clogging and adsorption of EBM onto enteral tubing surfaces, which Gaither et al demonstrated is a common occurrence for enteral feeding tubes.[18] Surface properties of polyurethane and silicone catheters such as hydrophobicity and their effects on particle adhesion have been compared extensively in the literature, and thus it may be hypothesized that these material properties could affect the volume of fat from EBM left behind in the tubing.[20]

Additionally, manufacturers of enteral feeding systems recently introduced the ENFit connection system in response to new International Organization for Standardization standards to enteral feeding systems, which aim to prevent accidental connection between enteral and nonenteral devices. This system standardizes the connection between the separate components of the feeding tube and syringe across feeding pump manufacturers.[21] Fat delivery of EBM using ENFit connections compared with the Legacy (traditional) connection has not yet been investigated, including the effects of changes in connection geometry on accurate delivery of fat from EBM through the enteral tubing. One change that could increase adsorption of fat is a small volume of additional dead space in the new connection.[22] This additional dead space may increase adsorption of milk fat globules, as Narayan et al demonstrated that longer tubing is associated with greater fat losses within tubing.[14]

Given the high variability of fat delivery in neonatal enteral feeding systems, a definitive study demonstrating the most effective means of optimizing fat delivery using currently available enteral feeding systems is needed. This study tests variables known to impact fat delivery from EBM using a simulated enteral feeding system at clinically relevant infusion rates of 5, 15, and 30 mL/h by comparing concentric and eccentric syringe systems, silicone and

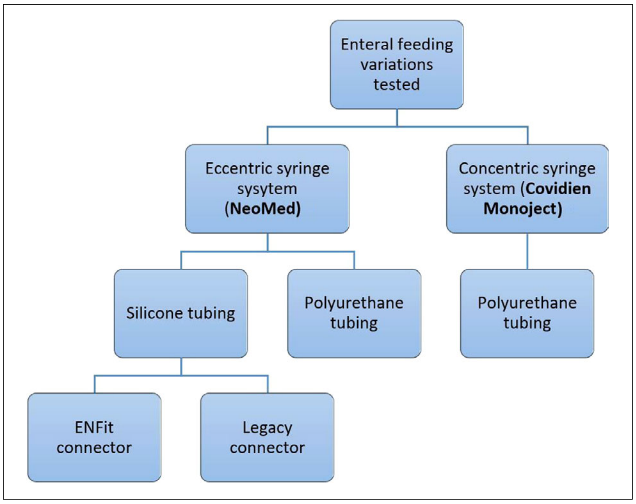

Figure 2. Flowchart of variations tested at 5-, 15-, and 30-mL/h infusion rates. ENFit connectors were used in all variations, with the exception of the comparison between ENFit vs Legacy connectors using eccentric silicone syringes.

polyurethane tubing materials, and the ENFit and Legacy connection systems.

Materials and Methods

Experimental Design

Variations tested were concentric vs eccentric syringes, polyurethane vs silicone tubing using eccentric syringes, and ENFit vs Legacy connectors using eccentric syringes with silicone tubing (Figure 2). Each combination of variables was tested at infusion rates of 5, 15, and 30 mL/h using 6-, 15-, and 35-mL syringes, respectively.

To accurately represent NICU enteral feeding in our laboratory, a simulated enteral feeding system was assembled. Smith's Medical (Minneapolis, MN) Medfusion Model 3500 pumps were attached to intravenous poles in the horizontal orientation using Smiths Medical pole clamps, and the syringes were tested with the feeding pump in the horizontal orientation at each infusion rate. Covidien Monoject (Dublin, Ireland) was used in the concentric system, and NeoMed (Woodstock, GA) was used for the eccentric system. NeoMed syringes were tested using both polyurethane and silicone nasogastric (NG) tubing, whereas Covidien syringes were tested using only polyurethane NG tubing because silicone NG tubing is not currently available in the Covidien system. The ENFit connection system was used for all variations, with the exception of the comparison between ENFit and Legacy connectors on eccentric syringes with silicone tubing.

EBM from 5 donors was thawed and warmed to 25°C in accordance with hospital milk bank protocols and then pooled in equal proportions prior to each set of experiments. The temperature of the pooled milk was then checked and rewarmed to 25°C as needed. An approximately 2-mL sample of this EBM was then collected and set aside prior to infusion for macronutrient content analysis. To prevent excessive fat loss because of repeated freeze-thaw cycles, excess EBM was discarded at the end of each set of experiments and a fresh batch of pooled EBM prepared for each day of experiments using the same technique.

Warmed EBM was loaded directly to fill Covidien Monoject concentric 6-, 12-, and 35-mL syringes and NeoMed eccentric 6-, 12-, and 35-mL syringes. EBM delivered using Covidien Monoject syringes was delivered through a Covidien 6.5-French (Fr) (51 cm) polyurethane NG tube. EBM delivered through NeoMed syringes was delivered via polyurethane 6.5-Fr (60 cm) tubing and silicone 6.5-Fr (60 cm) tubing for each syringe size and infusion rate. All simulated feedings were conducted at infusion rates of 5, 15, and 30 mL/h until the full volume of the syringe was infused. At the end of simulated feeds, EBM was collected in Corning (Corning, NY) Pyrex glass centrifuge tubes.

All analysis of fat content of EBM was conducted using the Unity SpectraStar (Milford, MA), which uses Fourier-transform infrared spectroscopy to calculate macronutrient concentration in human EBM. The 2-mL sample of pooled EBM collected prior to infusion was analyzed for fat content for each set of experiments, representing the baseline EBM macronutrient content prior to infusion. The collected EBM samples at the end of each simulated feed were analyzed for fat concentration.

Statistical Analysis

Each comparison was tested in triplicate because of the 3 different infusion rates. Because of variation in the fat content of pooled EBM prior to infusion, total fat delivery for each sample has been calculated and expressed as a percentage of total fat delivered relative to baseline fat content. The means and SD of the percent of fat content were calculated. Two-factor analysis of variance (ANOVA) models were fit to investigate associations of each factor of interest with fat delivery across infusion rates. After controlling for infusion rate, 3 separate two-factor ANOVA models were fit to examine the influence of the feeding system (eccentrics vs concentric), tubing (silicone vs polyurethane), and connection (ENFit vs Legacy) on fat delivery. Each of these ANOVA models was fit using both (1) fat delivery percentage relative to baseline and (2) total fat delivered in grams as the response variable, so a total of 6 ANOVA models were fit. A 2-sample *t*-test was used to make comparisons separately at each infusion rate, and a Bonferroni-adjusted significance level was used to control for multiple testing to maintain a 5% experiment-wise type I error rate. SAS version 9.4 (SAS Institute Inc, Cary, NC) was used for data analysis.

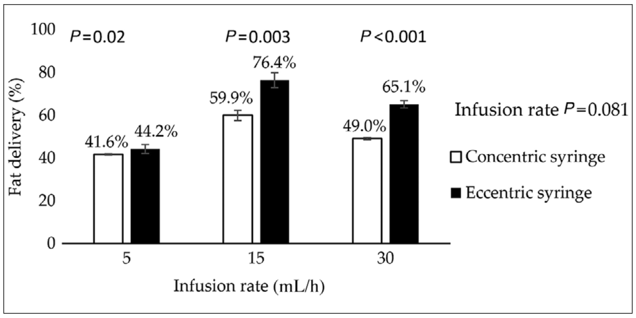

Figure 3. Comparison of fat delivery percentages of ENFit eccentric syringe and ENFit concentric syringe at 5-, 15-, and 30-mL/h infusion rates when using standard polyurethane tubing.

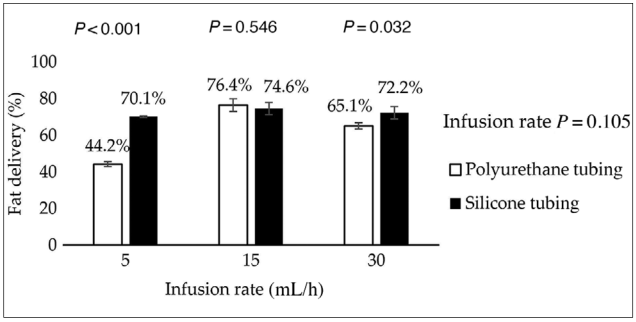

Figure 4. Comparison of fat delivery percentages of ENFit eccentric syringe with silicone and polyurethane nasogastric tubing at 5-, 15-, and 30-mL mL/h infusion rates.

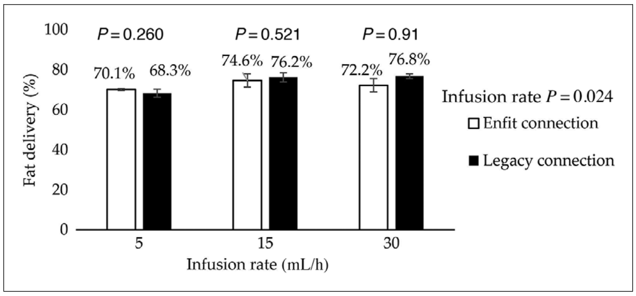

Figure 5. Comparison of fat delivery percentages of ENFit and Legacy connection systems using eccentric syringe with silicone nasogastric tubing at 5-, 15-, and 30-mL/h infusion rates.

Results

The percentage of fat delivery from EBM was first compared using polyurethane concentric and eccentric syringes with ENFit connectors (Figure 3). After controlling for infusion rate, fat delivery was 11.7% higher for the eccentric syringe system ($P = 0.036$) but did not vary significantly across infusion rates after controlling for type of syringe ($P = 0.081$). At an infusion rate of 5 mL/h, the eccentric syringe system showed improved fat delivery compared with the concentric syringe system (44.2 ± 0.1% and 41.6 ± 0.2%, respectively, $P = 0.029$), but this difference was not statistically significant using the Bonferroni-adjusted significance level of $\alpha = 0.017$ to control for multiple comparisons. The eccentric syringe system delivered a significantly higher fat percentage than the concentric syringe system at 15 mL/h (76.4 ± 3.5% and 59.9 ± 2.4%, respectively, $P = 0.003$) and 30 mL/h (65.1 ± 1.7% and 49 ± 0.4%, respectively, $P < 0.001$).

Fat delivery was then compared within the eccentric system using silicone and polyurethane enteral tubing (Figure 4). After controlling for infusion rate, fat delivery using silicone tubing was 10.4% higher than polyurethane tubing ($P = 0.039$) but did not vary significantly across infusion rates after controlling for the type of tubing ($P = 0.105$). At an infusion rate of 5 mL/h, silicone (70.1 ± 0.4%) provided significantly increased fat delivery compared with polyurethane tubing (44.2 ± 1.3%, $P < 0.001$), whereas no significant difference was found between silicone (74.6 ± 3.3%) and polyurethane tubing (76.4 ± 3.5%) at 15 mL/h ($P = 0.546$). At the rate of 30 mL/h, higher percentage of fat delivery was noted using silicone over polyurethane tubing (72.2% ± 3.4% and 65.1% ± 1.7%, respectively, $P = 0.032$), but this difference was not significant when using the Bonferroni-adjusted significance level of 0.017 to control for multiple comparisons.

Because the combination of eccentric with silicone tubing showed the best fat delivery from the tested variations, the ENFit connection system was compared with the traditional Legacy system using eccentric syringes with silicone tubing. As seen in Figure 5, no significant difference was found in the percent of fat delivery when comparing the Legacy and ENFit connectors across infusion rates ($P = 0.360$).

Discussion

Delivery of fat from EBM was found to be marginally improved with the eccentric syringe and silicone enteral tubing in the simulated continuous enteral feeds, suggesting that premature infants who are fed through this feeding system will receive a greater proportion of the calories found in EBM. This increase in caloric intake would be expected to improve outcomes in growth and neurodevelopment, and these outcomes should be further studied in prospective clinical trials using these improved enteral feeding systems.

The eccentric nozzle utilizes a flattened polypropylene plunger head and O-ring gasket that contributes not only to reducing fat adherence to the plunger head but also contributes to an increased proportion of fat travelling through the syringe tip into the tubing and ultimately to the infant. The “off-centered” position of the eccentric syringe nozzle facilitates the flow of EBM upwards, corresponding with the flow of fat that separates from the rest of the aqueous milk components. This allows for an additional hypothesis that reorienting the syringe and pump vertically will allow fat to be delivered earlier in the feed, as the fat molecule separates faster from the aqueous portion of milk in the vertical orientation and will "rise" to the top of the syringe. Limitation to performing this includes the Smiths Medical guidelines for the Medfusion pump, which do not recommend reorienting the pump.[23] However, further studies should consider testing this to optimize fat delivery.

Rogers et al hypothesized that there is greater adherence of fat to the delivery system when feeds are delivered at slower rates of infusion.[17] In their study, Rogers et al demonstrated that fat losses in continuous feeds were more substantial compared with gravity bolus feeds. These findings were replicated in our study, as increased fat delivery was associated with higher infusion rates (15 and 30 mL/h) between eccentric and concentric syringe systems in this study. Although this association was not found when comparing silicone vs polyurethane tubing, the substantially greater percentage of fat delivery with silicone at 5 mL/h showed that silicone is related to increased delivery of fat during slow infusion rates in which there is greater fat adherence.

Although our study demonstrated no significant difference between the ENFit and Legacy connection types for enteral feeding systems, these results may be expected since these connections have minimal contact with EBM during delivery and do not greatly affect the pattern of flow. Additionally, although the new ENFit connection has been shown to have additional dead space volume compared with the traditional Legacy connection, this volume is small and would not be expected to make a significant difference in the delivery of fat from EBM.

There is a need for continued design improvements and interventions in neonatal enteral feeding to decrease fat loss and optimize delivery. Further testing to compare enteral tube sizes looking at the length and the diameter of the tubing will be useful to evaluate which specific combinations deliver the greatest amount of fat from EBM. Comparing additional enteral feeding systems in the market by different manufacturers may be also be of interest to account for the variations used by different institutions.

This study has several limitations. First, although our experiment simulated continuous enteral feeds to best replicate the clinical setting, there may be discrepancies, as the final delivery of EBM in the simulation was collected in a glass centrifuge tube as opposed to delivery to premature infants in the clinical setting by bedside nurses. Additionally, our sample size is small, as we sought to test several configurations across multiple infusion rates using 2 feeding systems. Future studies could expand on these variations using a larger sample size, which would account for better power of results and potential significant results in other configurations.

Acknowledgments

NeoMed provided syringes and feeding tubes for this study (no research or monetary support).

Statement of Authorship

K. Abdelrahman, A. Hair, J. Jarjour, and D. Sutton contributed to conception/design of the research; K. Abdelrahman, A. Hair, J. Jarjour, D. Sutton, H. Yang, and J. Hagan contributed to acquisition, analysis, or interpretation of the data; K. Abdelrahman, J. Hagan, and J. Jarjour drafted the manuscript; K. Abdelrahman, A. Hair, J. Jarjour, D. Sutton, H. Yang, and J. Hagan critically revised the manuscript; and K. Abdelrahman, A. Hair, J. Jarjour, D. Sutton, H. Yang, and J. Hagan agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

References

1. Kim JH, Bode L, Ogra PL. Human milk. In: *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*. 8th ed. Philadelphia, PA: Elsevier/Saunders; 2016:189-213. Available at: https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323241472000055?scrollTo=%23hl0000914. Accessed January 21, 2019.
2. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. *Pediatr Clin North Am*. 2013;60(1):49-74, https://doi.org/10.1016/j.pcl.2012.10.002 Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3586783/ Accessed November 4, 2017.
3. Dusick AM, Poindexter BB, Ehrenkranz RA, Lemons JA. Growth failure in the preterm infant: can we catch up? *Semin Perinatol*. 2003;27(4):302-310. https://doi.org/10.1016/S0146-0005(03)00044-2
4. Robinson DT, Martin CR. Fatty acid requirements for the preterm infant. *Semin Fetal Neonatal Med*. 2017;22(1):8-14. https://doi.org/10.1016/j.siny.2016.08.009
5. Nutrient requirements and provision of nutritional support in the premature neonate. In Poindexter BB, Ehrenkranz RA. (eds.) *Fanaroff and Martin's Neonatal-Perinatal Medicine*. Amsterdam, the NEtherlands: Elsevier Health Sciences; 2010, 43, 592-612
6. Martin CR, Freedman SD. Lipid and fatty acid delivery in the preterm infant: challenges and lessons learned from other critically ill populations. In: *Gastroenterology and Nutrition: Neonatology Questions and Controversies*. 3rd ed. Philadelphia, PA: Elsevier; 2019:29-41. https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323545020000037?scrollTo=%23hl0000168. Accessed January 21, 2019.
7. Loÿs C-M, Maucort-Boulch D, Guy B, Putet G, Picaud J-C, Haÿs S. Extremely low birthweight infants: how neonatal intensive care unit teams can reduce postnatal malnutrition and prevent growth retardation. *Acta Paediatr*. 2013;102(3):242-248. https://doi.org/10.1111/apa.12092
8. Rayyan M, Rommel N, Allegaert K. The fate of fat: pre-exposure fat losses during nasogastric tube feeding in preterm newborns. *Nutrients*. 2015;7(8):6213-6223. https://doi.org/10.3390/nu7085279
9. Maruyama, H, Yonemoto, N. Weight growth velocity and neurodevelopmental outcomes in extremely low birth weight infants. *PLoS One*. 2015;10(9):e0139014, https://doi.org/10.1371/journal.pone.0139014
10. Demmelmair H, Koletzko B. Lipids in human milk. *Best Pract Res Clin Endocrinol Metab*. 2018;32(1):57-68. https://doi.org/10.1016/j.beem.2017.11.002

11. Su BH. Optimizing nutrition in preterm infants. *Pediatr Neonatol*. 2014;55(1):5-13. https://doi.org/10.1016/j.pedneo.2013.07.003 Available at: https://www.ncbi.nlm.nih.gov/pubmed/24050843 Accessed April 9, 2018.
12. Greer FR, McCormick A. Changes in fat concentration of human milk during delivery by intermittent bolus and continuous mechanical pump infusion. *J Pediatr*. 1984;105(5):745-749. Available at: https://www.ncbi.nlm.nih.gov/pubmed/6438286 Accessed November 5, 2017.
13. Martinez FE, Desai ID. Ultrasonic homogenization of expressed human milk to prevent fat loss during tube feeding. *J Pediatr Gastroenterol Nutr*. 1987;6(4):593-597. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3123636 Accessed November 5, 2017.
14. Narayanan I, Singh B, Harvey D. Fat loss during feeding of human milk. *Arch Dis Child*. 1984;59(5):475-477. https://doi.org/10.1136/adc.59.5.475
15. Tabata M, Abdelrahman K, Hair AB, Hawthorne KM, Chen Z, Abrams SA. Fortifier and cream improve fat delivery in continuous enteral infant feeding of breast milk. *Nutrients*. 2015;7(2):1174-1183. https://doi.org/10.3390/nu7021174
16. Stocks R, Davies D, Allen F, Sewell D. Loss of breast milk nutrients during tube feeding. *Arch Dis Child*. 1985;60(2):164-166.
17. Rogers SP, Hicks PD, Hamzo M, Veit LE, Abrams SA. Continuous feedings of fortified human milk lead to nutrient losses of fat, calcium and phosphorus. *Nutrients*. 2010;2(3); 230-240.
18. Gaither KA, Tarasevich BJ. Modification of polyurethane to reduce occlusion of enteral feeding tubes. *J Biomed Mater Res B Appl Biomater*. 2009;91(1), 135-142, https://doi.org/10.1002/jbm.b.31382. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19399855 Accessed November 5, 2017.
19. How NICU Syringe Choice Can Reduce Fat Loss In Human Breast Milk. Available at: http://www.NeoMedinc.com/wp-content/uploads/2016/02/NM-SMM-020-Rev-2-How-NICU-Syringe-Choice-Can-Reduce-Fat-Loss-in-Human-Breast-Milk.pdf Accessed November 5, 2017.
20. Jones DS, Garvin CP, Gorman SP. Relationship between biomedical catheter surface properties and lubricity as determined using textural analysis and multiple regression analysis. *Biomaterials*. 2004;25(7):1421-1428. https://doi.org/10.1016/j.biomaterials.2003.08.011
21. Small-bore connectors for liquids and gases in healthcare applications—Part 3: Connectors for enteral applications. Available at: https://www.iso.org/standard/50731.html Accessed November 5, 2017.
22. Guenter P. ENFit feeding tube connectors: a primer for the radiology nurse. *J Radiol Nurs*. 2016;35(4):296-299. https://doi.org/10.1016/j.jradnu.2016.10.004
23. *Medfusion Model 3500 Syringe Infusion Pump Operation Manual: Software Version 5.0*. St. Paul, MN: Smiths Medical ASD, Inc., 107. Available at: http://www.medfusionpump.com/assets/literature/manuals/Operators_Manual_3500_40-6370-01A.pdf Accessed November 6, 2017.